SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Attia 200 mg Modified-Release Capsules, Hard

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each modified-release capsule contains dipyridamole 200 mg.

Excipients: The capsules also contain ponceau 4R (E124). For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Modified-release capsule, hard.

Yellow to orange coloured pellets filled in size “0xel” hard capsules with opaque dark red cap and opaque dark orange body, imprinted ‘DPM’ on cap and ‘200’ on body with white ink.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

- Secondary prevention of ischaemic stroke and transient ischaemic attacks either alone or in conjunction with aspirin.
- An adjunct to oral anti-coagulation for prophylaxis of thromboembolism associated with prosthetic heart valves.

4.2 Posology and method of administration

For oral administration

Adults, including the elderly
The recommended dose is one capsule twice daily, usually one in the morning and one in the evening preferably with meals.
The capsules should be swallowed whole without chewing.

**Children**
Attia is not recommended for children.

**Alcohol**
Attia should not be taken at the same time as an alcoholic beverage (see section 4.5).

### 4.3 Contraindications

Hypersensitivity to any component of the product

### 4.4 Special warnings and precautions for use

Among other properties, dipyridamole acts as a potent vasodilator. It should therefore be used with caution in patients with severe coronary artery disease including unstable angina and/or recent myocardial infarction, left ventricular outflow obstruction or haemodynamic instability (e.g. decompensated heart failure).

Patients being treated with regular oral doses of Attia should not receive additional intravenous dipyridamole. Clinical experience suggests that patients being treated with oral dipyridamole who also require pharmacological stress testing with intravenous dipyridamole, should discontinue drugs containing oral dipyridamole for twenty-four hours prior to stress testing.

In patients with myasthenia gravis readjustment of therapy may be necessary after changes in dipyridamole dosage (See Interactions).

Attia should be used with caution in patients with coagulation disorders.

Attia capsules contain ponceau 4R (E124), a colouring agent, which may cause allergic reactions.

### 4.5 Interaction with other medicinal products and other forms of interaction

Dipyridamole increases the plasma levels and cardiovascular effects of adenosine. Adjustment of adenosine dosage should therefore be considered if use with dipyridamole is unavoidable.

There is evidence that the effects of acetylsalicylic acid and dipyridamole on platelet behaviour are additive.
When dipyridamole is used in combination with anticoagulants or acetylsalicylic acid, the statements on intolerance and risks for these preparations must be observed. Addition of dipyridamole to acetylsalicylic acid does not increase the incidence of bleeding events. When dipyridamole was administered concomitantly with warfarin, bleeding was no greater in frequency or severity than that observed when warfarin was administered alone.

Dipyridamole may increase the hypotensive effect of blood pressure lowering drugs and may counteract the anticholinesterase effect of cholinesterase inhibitors thereby potentially aggravating myasthenia gravis.

Attia should not be taken at the same time as alcohol, as alcohol may increase the rate of release of dipyridamole from the modified-release preparation.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is inadequate evidence of safety in human pregnancy, but dipyridamole has been used for many years without apparent ill-consequence. Animal studies have shown no hazard. Nevertheless, medicines should not be used in pregnancy, especially the first trimester unless the expected benefit is thought to outweigh the possible risk to the foetus (see section 5.3).

Lactation
Attia should only be used during lactation if considered essential by the physician.

Fertility
No studies on the effect on human fertility have been conducted with dipyridamole. Non-clinical studies with dipyridamole did not indicate direct or indirect harmful effects with respect to fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

None stated.

4.8 Undesirable effects

Adverse reactions at therapeutic doses are usually mild. Vomiting, diarrhoea and symptoms such as dizziness, nausea, dyspepsia, headache and myalgia have been observed. These tend to occur early after initiating treatment and may disappear with continued treatment.
As a result of its vasodilating properties, Attia may cause hypotension, hot flushes and tachycardia. Worsening of the symptoms of coronary heart disease such as angina and arrhythmias.

Hypersensitivity reactions such as rash, urticaria, severe bronchospasm and angioedema have been reported. In very rare cases, increased bleeding during or after surgery has been observed.

Isolated cases of thrombocytopenia have been reported in conjunction with treatment with dipyridamole.

Dipyridamole has been shown to be incorporated into gallstones.

4.9 Overdose

Symptoms
Due to the low number of observations, experience with dipyridamole overdose is limited. Symptoms such as feeling warm, flushes, sweating, accelerated pulse, restlessness, feeling of weakness, dizziness, drop in blood pressure and anginal complaints can be expected.

Therapy
Symptomatic therapy is recommended. Administration of xanthine derivatives (e.g. aminophylline) may reverse the haemodynamic effects of dipyridamole overdose. ECG monitoring is advised in such a situation. Due to its wide distribution to tissues and its predominantly hepatic elimination, dipyridamole is not likely to be accessible to enhanced removal procedures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
The antithrombotic action of dipyridamole is based on its ability to modify various aspects of platelet function such as inhibition of platelet adhesion and aggregation, which have been shown to be factors associated with the initiation of thrombus formation, as well as lengthening shortened platelet survival time.

5.2 Pharmacokinetic properties
Dipyridamole 200 mg modified-release capsules given twice daily has been shown to be bioequivalent to the same total daily dose of Dipyridamole Tablets given in four divided doses.

Peak plasma concentrations are reached 2 - 3 hours after administration. Steady state conditions are reached within 3 days.

Metabolism of dipyridamole occurs in the liver predominantly by conjugation with glucuronic acid to form a monoglucuronide. In plasma about 70 - 80% of the total amount is present as parent compound and 20 - 30% as the monoglucuronide.

Renal excretion is very low (1 - 5%).

5.3 Preclinical safety data

Dipyridamole has been extensively investigated in animal models and no clinically significant findings have been observed at doses equivalent to therapeutic doses in humans.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Contents:
Tartaric acid
Hyromellose
Povidone
Acacia
Talc
Methacrylic acid-methyl methacrylate copolymer (1:2)
Hyromellose phthalate
Dimethicone
Triacetin
Stearic acid

Capsule Shells (HPMC):
Hyromellose
Brilliant blue (E133)
Ponceau 4R (E124)
Quinoline yellow (E104)
Titanium dioxide (E171)
Potassium Acetate
Carrageenan
Printing Ink:
Shellac
Potassium Hydroxide
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

In-use: 15 days

6.4 Special precautions for storage

Store in the original package in order to protect from moisture. Keep the bottle tightly closed.
This medicinal product does not require any special temperature storage precautions.

6.5 Nature and contents of container

White HDPE bottle with child resistant plastic cap with molecular sieve pillow pouch as a desiccant.
Packs contain 30 or 60 capsules. Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements

7 MARKETING AUTHORISATION HOLDER

Dr. Reddy’s Laboratories (UK) Ltd.
6 Riverview Road
Beverley
8 MARKETING AUTHORIZATION NUMBER(S)

PL 08553/0458

9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORIZATION

31/08/2012

10 DATE OF REVISION OF THE TEXT

31/01/2014